

### **REMARKS**

Claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, and 116-123 are pending. Claims 13, 15, 16, 18, 21, 23, 33, 45, 46, 50, 85, 87, 88, 89, 90, 91, 92, 93, 94, 100, 101, 102, and 122 have been amended. Claims 25-27, 35-37, 52, 55, 56, 61, 62, 65-67, 69-71, 73-75, 79-84, 86, and 113-115 have been cancelled without prejudice to or disclaimer of the underlying subject matter. Claims 1-12, 14, 22, 24, 34, 38, 40-44, 47-49, 51, 63, 64, 68, 72, 95, and 99 were previously cancelled without prejudice to or disclaimer of the underlying subject matter. Claims 124-130 have been added. Upon entry of the foregoing amendment, claims 13, 15-21, 23, 28-33, 39, 45, 46, 50, 53, 54, 57-60, 76-78, 85, 87-94, 96-98, 100-112, and 116-130 will be pending. Support for the new and amended claims can be found throughout the specification and claims as originally filed, for example on page 16, lines 30-34; page 17, line 30 through page 18, line 2; and page 49, line 14 through page 51, line 35. No new matter enters by way of this amendment.

#### ***1. Election/Restrictions***

Applicants acknowledge the finality of the restriction requirement but maintain their traversal. To facilitate prosecution, however, Applicants have cancelled, without prejudice or disclaimer to the underlying subject matter, the non-elected claims from the application. Applicants specifically reserve the right to file a divisional application directed to the non-elected subject matter.

#### ***2. Information Disclosure Statement***

Applicants respectfully thank the Examiner for returning the Examiner-initialed copies of Form PTO-1449 filed on January 3, 2005, and indicating that the "information referred to therein has been considered as to the merits." Office Action at page 2.

#### ***3. Withdrawn Objections and/or Rejections***

Applicants respectfully thank the Examiner for indicating that the "objection to claims 13, 90, 92 and 93 as set forth at page 8 of the previous Office Action (15 June 2004) is withdrawn." *Id.*

#### **4. Claim Rejections Under 35 U.S.C. § 112, First Paragraph, Enablement**

Claims 109, 112, and 119 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way so as to enable those skilled in the art to make and/or use the invention. Office Action at page 3. This rejection is respectfully traversed for at least the reasons which follow.

The Examiner asserts that “while PYY may be treating altered glucose metabolism in an animal suffering from hyperlipidemia or hyperlipoproteinemia, the results from Exhibit C do not demonstrate PYY actually treating hyperlipidemia or hyperlipoproteinemia” and concludes that the “scientific reasoning as a whole indicates that the rejection should be maintained.” Office Action at page 4. Applicants respectfully traverse this rejection.

Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to practice the claimed invention without undue experimentation. For example, the specification discusses the use of PYY in methods for treating subjects having altered glucose metabolism and associated disease states, including hyperlipidemia and hyperlipoproteinemia. *See Specification*, page 12, lines 14-17. In addition, the specification provides examples of the ability of PYY, PYY agonists and biologically active fragments thereof to rescue glucose responsiveness in pancreatic cells. *See Specification*, at page 49, line 14, *et seq.*, under the heading “Exemplification.” Moreover, Applicants have presented additional evidence of PYY’s ability to control glucose in rats predisposed to diabetes. *See Exhibit C* and related arguments provided in Applicants’ Response submitted December 15, 2004.

From such teachings the skilled artisan would recognize that such ability to enhance glucose responsiveness in cells would also be useful in treating related conditions such as hyperlipidemia and hyperlipoproteinemia in subjects having altered glucose metabolism. For example, Randle summarizes some of the knowledge the skilled artisan possesses regarding the association of altered glucose metabolism with plasma lipid levels. More specifically, the reference discusses an association between altered glucose metabolism and lipid metabolism. *See, e.g., Randle, P.J., Diabetes/Metabolism Rev. (1998) 14:263-283.* There is extensive discussion of studies investigating the reciprocal relationship of glucose metabolism and fatty acid metabolism. It is well established that in the context of enablement a patent application

“need not teach, and preferably omits, what is well known in the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) citation omitted. Further, as set forth above, the specification discusses the use of PYY and PYY agonists and biologically active fragments thereof for the treatment of hyperlipidemia and hyperlipoproteinemia. Taken in combination with the knowledge of those skilled in the art, the specification provides adequate guidance regarding the identification of subjects with altered glucose responsiveness, and the treatment of hyperlipidemia and hyperlipoproteinemia.

The Examiner argues, however, that the effects of PYY in a Zucker Diabetic Fatty rat “could correlate with treating diseases/conditions such as insulin resistance, glucose intolerance, glucose non-responsiveness or Type II diabetes mellitus, however, the results... are not applicable to treating hyperlipidemia or hyperlipoproteinemia.” Office Action at page 4. The Examiner has not provided any evidence that the results are not applicable to treating hyperlipidemia or hyperlipoproteinemia. The skilled artisan reading the instant disclosure would recognize that the methods can be used for treating such conditions in subjects having altered glucose responsiveness.

As such, it is submitted that Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary skill in the art to practice the invention without undue experimentation. The Examiner has not provided sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Examiner has provided generalizations regarding a lack of predictability in the art.

Accordingly, for at least these reasons, it is submitted that claims 109, 112, and 119 are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

Claims 13, 21, 23, 33, 45, 87-94, and 102 also remain rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way so as to enable those skilled in the art to make and/or use the invention. Office Action at page 3. The Examiner maintains that “while being enabling for the instant methods wherein a PYY agonist or biologically active fragment thereof has the following functions of PYY (a) binds a PYY receptor and (b) promotes glucose-responsiveness of

pancreatic islets or pancreatic cells and optionally (c) inhibits intestinal motility or (d) inhibits mesenteric blood flow; or (e) mediates gastric, pancreatic, or intestinal exocrine secretion; or (f) stimulates net absorption of nutrients,” the Examiner argues that the specification “does not reasonably provide enablement for: the instant methods wherein a PYY agonist or biologically active fragment thereof has one or more of the following functions of PYY.” Office Action at pages 4-5. Applicants disagree<sup>1</sup> but, to facilitate prosecution, have amended the claims to recite that the PYY agonist or biologically active fragment binds a PYY receptor or promotes glucose-responsiveness of a pancreatic cell.

Applicants have provided considerable direction and guidance, and have presented working examples. For example, the specification discusses PYY agonists and biologically active fragments. *See Specification*, page 21, line 30 through page 23, line 17. The specification also discusses that such “biological activity includes the induction or enhancement of glucose responsivity.” *See Specification*, page 23, lines 8-9. Moreover, the specification provides methods for identifying enhanced glucose responsiveness, as well as working examples of enhanced glucose responsiveness. *See Specification*, page 23, lines 9-12 and page 49, line 14, *et seq.* under the heading “Exemplification.” The specification further discloses compounds that bind to PYY receptors such as the PYY Y1 receptor. *See Specification*, page 6, lines 23-29 and page 10, line 21 through page 11, line 2. Taken in combination, such disclosure provides adequate direction to those skilled in the art of how to make and use the claimed invention as currently amended.

In addition, the skilled artisan is well-aware of PYY receptors and methods for determining PYY receptor binding. For example, Gehlert provides a summary of some of the knowledge the skilled artisan possesses of PP family receptors and their affinity for PP family member proteins. *See*, Gehlert, D.R., *Proc. Soc. Exp. Biol. Med.* (1999) 218(1):7-22. Gehlert reviews studies investigating PYY receptors and assays categorizing such receptors, for example by their ability to mediate the inhibition of adenylate cyclase. It is well established that in the context of enablement that a patent application “need not teach, and preferably omits, what is

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<sup>1</sup> Applicants respectfully submit that the Examiner has not provided specific evidence to cast doubt on the guidance provided in the specification but rather is relying upon generalizations regarding “the large quantity of experimentation necessary to induce/enhance glucose-responsiveness of impaired pancreatic islets and pancreatic cells, induce/enhance glucose metabolism in an animal and maintain/restore normal pancreatic islet function.” Office Action at page 6.

well known in the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) citation omitted. The teachings of the present specification taken in combination with the knowledge of those skilled in the art, the specification provides adequate guidance regarding the identification of PYY peptides, agonists and biologically active fragments thereof that bind to a PYY receptor for use in the claimed methods.

In this regard, based on the teachings of the present specification and the knowledge of those skilled in the art, a skilled artisan is more than capable of making or using the claimed invention as currently amended. Accordingly, for at least these reasons, it is submitted that claims 13, 21, 23, 33, 45, 87-94 and 102 are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and reconsideration and withdrawal of this rejection is respectfully requested.

#### ***5. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph***

Claims 13, 21, 23, 33, 45, 87, 92, 93, and 122 stand rejected under 35 U.S.C. §112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Withdrawal of these rejections is respectfully requested for at least the reasons which follow.

Claims 13, 45, 87, and 92 are allegedly indefinite due to the recitation of the phrase “pancreatic islet or cell.” Although Applicants disagree, claims 13, 45, 87, and 92 have been amended to recite “pancreatic cell.” Accordingly, it is submitted that the claims comply with 35 U.S.C. § 112, second paragraph, and withdrawal of this rejection is respectfully requested.

Claims 13, 21, 23, 33, 45, and 93 are allegedly indefinite due to recitation of the phrase “an amino acid sequence having a corresponding nucleic acid sequence.” *Office Action* at pages 6-7. Although Applicants disagree that such a phrase is indefinite when read in light of the specification, claims 13, 21, 23, 33, 45, and 93 have been amended to recite “an amino acid sequence having a sequence identical to a peptide encoded by a nucleic acid sequence wherein the nucleic acid sequence hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to SEQ ID NO: 1.” As such, withdrawal of this rejection is respectfully requested.

Claim 122 is allegedly indefinite “in the recitation of amino acid positions (or nucleotide sequences) in the absence of a referenced SEQ ID NO:.” Although Applicants disagree that such a phrase is indefinite when read in light of the specification, claim 122 has been amended to

recite that the recited PYY refers to the positions “of SEQ ID NO: 3.” As such, withdrawal of this rejection is respectfully requested.

**6. Claim Rejections Under 35 U.S.C. § 102(b)**

Claims 23, 89, 102-105, 108, 111, and 118 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Morley *et al.*, Life Sciences, Vol. 41, pg 2157-2165 (1987) (“Morley *et al.*”). This rejection is respectfully traversed and reconsideration is requested for at least the reason that follow.

The Examiner alleges that

Morley *et al.* teach the administration of PYY to mice (page 2158, last paragraph). Morley *et al.* teach that the peripheral administration of peptide YY (PYY) caused weight loss (abstract; page 2158 last paragraph and Table 5). Morley *et al.* state that neurotransmitters that enhance feeding centrally cause weight loss when given peripherally. Morley *et al.* state that this is best demonstrated in this study where PYY caused weight loss. Morley *et al.* teach that PYY caused weight loss, without altering food intake (page 2163, last paragraph-page 2164, first paragraph).

*Office Action* at page 8.

Morley *et al.* fails to disclose all of the limitations of the present claims. “It is axiomatic that for prior art to anticipate under § 102 it has to meet every element of the claimed invention.” *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). The cited reference fails to specifically teach, disclose or suggest methods for treating a disease associated with altered glucose metabolism by administering PYY or PYY agonist or a biologically active fragment to *an animal having a disease associated with altered glucose metabolism*. Morley *et al.* discusses the administration of anorexigenic drugs to mice (TAC/SW). Morley *et al.*, at page 2158. The Examiner has not pointed to any disclosure in Morley *et al.* that such mice have a disease associated with glucose metabolism. As such, whatever else Morley *et al.* discloses, it fails to teach, disclose or even suggest a method for treating a disease associated with altered glucose metabolism as currently claimed.

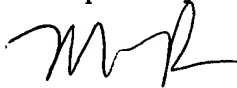
Accordingly, the rejection of claims 23, 89, 102-105, 108, 111, and 118 under 35 U.S.C. § 102(b) is traversed. Reconsideration and withdrawal of this rejection are respectfully requested.

**CONCLUSION**

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under Order No. CIBT-P01-058.**

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Respectfully Submitted,



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